

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

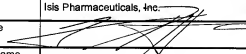
Total Number of Pages in This Submission 6

Patent Number	7,125,975
Issue Date	10/24/2006
First Named Inventor	Muthiah Manoharan
Title	DERIVATIZED OLIGONUCLEOTIDES HAVING IMPROVED UPTAKE AND OTHER PROPERTIES
Attorney Docket Number	ISIS-5425

ENCLOSURES (Check all that apply)

<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD <input type="checkbox"/> Remarks	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Certificate of Correction
--	--	---

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Isis Pharmaceuticals, Inc.		
Signature			
Printed name	Herb Boswell		
Date	11/13/2006	Reg. No.	27,311

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 5

PATENT NO. : 7,125,975

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

1) Title Page:

Item [60], Related U.S. Application Data, please delete

"Continuation of application No. 10/073,718, filed on Feb. 11, 2002, now Pat. No. 6,831,166, which is a division of application No. 09/633,659, filed on Aug. 7, 2000, now Pat. No. 6,395,492, which is a division of application No. 08/211,882, filed on Apr. 22, 1994, now Pat. No. 6,153,737, which is a continuation-in-part of application No. PCT/US92/09196, filed on Oct. 23, 1992."

and insert therefore

--Continuation of application No. 10/073,718, filed on Feb. 11, 2002, now Pat. No. 6,831,166, which is a division of application No. 09/633,659, filed on Aug. 7, 2000, now Pat. No. 6,395,492, which is a division of application No. 08/211,882, filed as application No. PCT/US92/09196 on Oct. 23, 1992, now Pat. No. 6,153,737.--;

2) Column 6, line 21, please delete "B6" and insert therefore --B₆--;

3) Column 9, line 61, please delete " ";

4) Column 10, line 12, please delete "--";

5) Column 10, line 54, please delete "Bas" and insert therefore --Base--;

6) Column 11, line 58, please delete "." after "treated";

7) Column 12, line 13, please delete "C₅T₅G₅ T₅C₅T₅ C₅C₅A₅ T₅C₅C₅ T₅C₅T₅ T₅C₅A₅ C₅T" and insert therefore --C₅T₅G₅ T₅C₅T₅ C₅C₅A₅ T₅C₅C₅ T₅C₅T₅ T₅C₅A₅ C₅T--;

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Isis Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

Page 2 of 5

PATENT NO. : 7,125,975

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

8) Column 15, line 47, please delete "is" and insert therefore --"s"--;

9) Column 17, line 14, please delete " Na_2CO_3 ,M" and insert therefore -- Na_2CO_3 /1M--;

10) Column 17, line 44, please delete " Na_2HCO_3 ,M" and insert therefore -- Na_2HCO_3 /1M--;

11) Column 19, please delete

TABLE 1

HPLC Retention Times Of Oligonucleotides Functionalized
At 2' Position

Oligomer	Retention Time Minutes	
	Mono Substitution	Multiple Substitution
Oligomer 12 ¹	21.78	
Oligomer 13 ¹	22.50	
Oligomer 19 ²	23.58	
Oligomer 20 ²	24.16 ^a	25.19 ^b
Oligomer 21 ³	26.65	
Oligomer 22 ³	26.99 ^a	29.33 ^b
	27.55 ^a	
Oligomer 23 ⁴	30.10	
Oligomer 24 ⁴	30.38 ^a	37.00 ^b
	32.22 ^a	
Oligomer 25 ⁵	28.06	
Oligomer 26 ⁵	28.14 ^a	33.32 ^b
	29.24 ^a	

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Isis Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 3 of 5

PATENT NO. : 7,125,975

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

and insert therefore

TABLE 1

HPLC Retention Times Of Oligonucleotides Functionalized
At 2' Position

Oligomer	Retention Time Minutes	
	Mono Substitution	Multiple Substitution
Oligomer 12 ¹	21.78	
Oligomer 13 ¹		22.50
Oligomer 19 ²	23.58	
Oligomer 20 ²		24.16 ^a 25.19 ^b
Oligomer 21 ³	26.65	
Oligomer 22 ³		26.99 ^a 29.33 ^b 27.55 ^a
Oligomer 23 ⁴	30.10	
Oligomer 24 ⁴		30.38 ^a 37.00 ^b 32.22 ^a
Oligomer 25 ⁵	28.06	
Oligomer 26 ⁵		28.14 ^a 33.32 ^b 29.24 ^a

--;

12) Column 21, line 14, please delete "Prot in-Conjugated" and insert therefore --Protein-Conjugated--;

13) Column 21, line 27, please delete ""is"" and insert therefore --"s"--;

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Isis Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 4 of 5

PATENT NO. : 7,125,975

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

14) Column 22, please delete

TABLE 2
OLIGONUCLEOTIDE ANALYSIS VIA ENZYMATIC DIGESTION

Oligomer	<u>Observed Ratios</u> ^{**}				
	Abs. max.	267	252	267	260
	C	G	T	A	A
Oligomer 10	2	1		1	
Oligomer 11	3	5	2	1	
Oligomer 12	9	1	8	1	1
Oligomer 13	9	1	8	2	

And insert therefore

TABLE 2
OLIGONUCLEOTIDE ANALYSIS VIA ENZYMATIC DIGESTION

Oligomer	<u>Observed Ratios</u> ^{**}				
	Abs. max.	267	252	267	260
	C	G	T	A	A
Oligomer 10	2	1		1	
Oligomer 11	3	5	2	1	
Oligomer 12	9	1	8	1	1
Oligomer 13	9	1	8	2	

15) Column 24, line 46, please delete "phase-HPLC" and insert therefore --phase HPLC--;

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Isis Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

**UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION**

Page 5 of 5

PATENT NO. : 7,125,975
APPLICATION NO.: 10/755,166
ISSUE DATE : 10/24/2006
INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- 16) Column 29, line 7, please delete "solution-of" and insert therefore --solution of--;
- 17) Column 39, line 19, please delete "3" and insert therefore --30--;
- 18) Column 46, Claim 5, lines 32-33, please delete "5'-position" and insert therefore --5'-O-position--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Isis Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**